Details of the Project sanctioned under the Human Resource Development scheme of Department of Health Research

1. **Project Title:** Proteomic analysis of retinoblastoma and HPV associated biological pathways

2. **Category of fellowship: DHR/ HRD/ Start up grant**

3. **PI (Name & Address):** Dr Ritu Aggarwal, Professor, Deptt of Immunopathology, PGIMER, Chandigarh

4. **Qualifications : M.D, DNB (Pathology)**

5. **Co.PI (Name & Address):** 1. Professor Usha Singh, Deptt of Opthalmology, PGIMER, Chandigarh

   2. Professor Deepak Bansal, Deptt of Pediatrics, APC, PGIMER, Chandigarh

6. **Duration of the project : Three years**

7. **Broad area of Research: Cancer**

   7.1 **Sub Area : Retinoblastoma**

8. **Summary of the Project:** (Give in about 300 words)

Summary of the proposed proposal

1. Retinoblastoma is the most common cancer of eye in children. Majority (95%) of cases occur below the age of 5 years.
2. The incidence is believed to be higher in developing countries including India. Children from lower socioeconomic status have a higher susceptibility.
3. Etiology of non – inherited retinoblastoma is unclear. There is increasing evidence of association with HPV. The retinoblastoma gene (pRb) has been reported to be abrogated by oncogenic proteins produced by several viruses including HPV.
4. In an important observation, the incidence of retinoblastoma has been found to parallel the incidence of cervical cancer in the world suggesting that an infective

organism may be a common etiological agent. This is a significant concept as vaccines are commercially available for various HPV subtypes.

5. Role of HPV in the pathogenesis of cervical and oral cancer is proven, but its pathogenesis in retinoblastoma is unclear.

6. HPV has been reported to induce post translational interactions of oncoproteins E6 and E7 with. Inactivation of cell cycle regulatory proteins p53 and pRB follows.

7. Proteomics is the study of the complete set of proteins expressed by a genome that helps in the identification of various disease-specific targets and uncovers new endpoints for the evaluation of chemopreventive agents and protein based drug targets for better treatment.

8. Protein profiling of retinoblastoma with co-existing HPV has not been reported in the literature till date.

9. Taking advantage of the high throughput proteomic profiling techniques, the study will be performed with two dimensional gel electrophoresis (2-DE) and mass spectrometry (MS) to study the protein profile of HPV positive and negative retinoblastoma tumor tissue as well as normal retinal tissue

10. It is plausible that the study may lead to establishment of novel protein biomarkers that may have diagnostic and therapeutic implications.

9. Objectives of the Proposal:

The **objectives** are

1. To study the comparative proteomic analysis of retinoblastoma tumor tissue and normal retina
2. To ascertain the exposure of HPV subtypes with linear array HPV genotyping assay in retinoblastoma
3. To study the differential protein profile of HPV positive and negative retinoblastoma tumor tissue
4. To study the mRNA expression of selected proteins by quantitative real-time PCR and to correlate the protein expression with mRNA expression

11. Innovations in the project: (Give in about 100 words)

The study will provide a more comprehensive picture of protein changes in response to pathological stress (HPV induced) for disease progression as compared to controls. It

is plausible that the study may lead to establishment of novel protein biomarkers that may have therapeutic implications. The novel proteins identified in the study will be studied for their therapeutic efficacy and will be tested in the primary culture. This futuristic approach will lead us to therapeutic targets which can be used as adjunct therapy. This has the potential to increase the efficacy of the existing regimen and decrease the toxicity.

11. Significance of the outcome of the project: (Give in about 150 words)

Retinoblastoma is the most common cancer of eye in children. Majority (95%) of cases occur below the age of 5 years. The incidence is believed to be higher in developing countries including India. Children from lower socioeconomic status have a higher susceptibility. The need of the hour is to develop therapeutic strategies which can help in preserving the vision of the child. It is imperative to find novel therapeutic target which have higher efficacy and are less toxic. The study utilizes a proteomic approach to study the differential protein profile in HPV positive and negative retinoblastoma tumor tissue. This approach will have in understanding the differential protein profile and identify novel proteomic biomarkers in response to pathogenic stress which would facilitate retinoblastoma treatment and prognosis.

12. Relevance in Public Health:

- The role of HPV in the pathogenesis of several diseases has been well established but its role in disease manifestation in retinoblastoma is still controversial. The present study will highlight the role of HPV in the pathogenesis of retinoblastoma. This is important since prophylactic vaccines are available for various HPV subtypes.
- With the advancement in proteomic technology, a target approach for the treatment of tumours can be foreseen. The present study will employ a comparative proteomic approach to identify certain novel proteomic biomarkers in response to pathogenic stress which would facilitate retinoblastoma treatment and prognosis.

Signature of the Fellow /Faculty